1626

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Date October 28, 2003 **Pages including cover** 14

Subject **Petition to the Commissioner Under 37 C.F.R. 1.144**

Serial No.: 10/019,976
Filing Date: October 23, 2001
Applicant: Bigham et al.
Title: Imidazoline Derivatives as Alpha-1A Adrenoceptor Ligands

Attached:
Certificate of transmission via facsimile
Petition to the Commissioner Under 37 C.F.R. 1.144

Thank you,
Valerie Phillips

Certificate of Transmission by Facsimile (37 CFR 1.8)

I hereby certify that this Response to Office Action is being facsimile transmitted to the United States Patent and Trademark Office (Fax. No. 703-308-6196) on October 28, 2003.

Valerie L. Phillips

Valerie L. Phillips

PU3650-USw

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Bigham, et al.
Filed: October 23, 2001 Art Unit: 1626
Serial No.: 10/019,976 Examiner: G. Shameem
For: Imidazoline Derivatives As Alpha-1A Adrenoceptor Ligands

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO THE COMMISSIONER UNDER 37 C.F.R. 1.144

Sir:

This is a petition of the final office action maintaining an objection of Claims 1-17, 19, and 20. This final action was mailed September 15, 2003. Since this final action is characterized solely as an objection, Applicants may not be able to appeal to the Board. In addition, this is a situation in which the supervisory authority of the Commissioner is appropriate. Therefore, this Petition is proper under 37 C.F.R. § 1.144 and 1.181. Applicants hereby petition the Commissioner to take the following action.

I. POINTS TO BE REVIEWED

The Commissioner is requested to review the propriety of the Examiner's actions with respect to the Restriction Requirement, Election of Species and refusal to examine claims as more precisely set forth in Sections II, III and IV below.

II. ACTION REQUESTED

Petitioner hereby requests

(1) that the Commissioner order the Examiner to withdraw the objections to the claims set forth in the Office Action mailed September 15, 2003;

(2) that the Commissioner order the Examiner to examine the entire scope of claims 1-17, 19 and 20; and

(3) that, to the extent that the PTO rules (Title 37 – Code of Federal Regulations Patents, Trademarks, and Copyrights) or the procedures set forth in the Manual of Patent Examining Procedure (MPEP) are inconsistent with the patent laws (Title 35 of the United States Code), are inconsistent with controlling case law or deprive the applicant of due process, the relevant PTO rules and/or procedures be withdrawn.

III. STATEMENT OF THE FACTS

(1) The claims of the present application are set forth in Appendix 1.

(2) The Examiner made an oral restriction requirement between Group I (claims 1-13 and 19-20), Group II (claims 14-17, and Group III (Claims 24-29) on or about April 14, 2003.

(3) The Examiner also required an election of species of a single disclosed species (compound) for examination on or about April 14, 2003.

(4) Applicants orally elected Group I with traverse on or about April 14, 2003, and confirmed the election with traverse in writing on June 19, 2003.

(5) Applicants orally elected the species of claim 13 on or about April 14, 2003, and confirmed this election in writing on June 19, 2003.

(6) On April 25, 2003, the Examiner issued an Office Action wherein he indicated that the elected species of claim 13 was allowable.

(7) In the Office Action of April 25, 2003, the Examiner also identified a "generic concept" that would be allowable (see the section entitled, "***Status of Claims***" bridging pages 5 and 6 of the Office Action).

(8) This "generic concept" does not encompass the entire scope of claim 1.

(9) On June 19, 2003, Applicants' representative requested reconsideration of the requirement and asked the Examiner to extend the search to the additional subject matter claimed in claim 1.

(10) On September 15, 2003, the Examiner issued a "Final Action" in which it was indicated that the Examiner would consider rejoining method of use claims 14-17 commensurate in scope with the product claims when the case is in condition for allowance (see the top of page 3 of the Office Action).

(11) However, the Examiner refused to examine the full scope of claim 1 and made the "Restriction Requirement" final (see the bottom of page 3 of the

Office Action). Thus, there has been a proper request for reconsideration (37 C.F.R. 1.144) and repeated action by the Examiner (37 C.F.R. 1.181(c)).

(12) Claim 1 encompasses a number of compounds that are alpha-1A agonists (see page 1, lines 7-9 and page 3, lines 24-28 of the specification).

(13) Compounds of the invention are useful in treating alpha-1A mediated diseases (see page 3, lines 25-34 of the specification), and in particular urinary incontinence (see page 1, lines 7-9 and page 3, line 30 of the specification).

IV. BRIEF IN SUPPORT OF PETITION

A. Applicants' have a right to an examination of the claims presented on their merits and the actions of the Examiner deprive applicants of due process.

An applicant is given the right to claim his/her invention in a manner which complies with the statutory requirements of the patent laws, In re Weber, 198 USPQ 328, 331 (CCPA 1978). This right has been recognized as a "basic right", In re Weber, supra, at 198 USPQ 332. If a claim does not comply with the patent laws, a rejection can be made. The Examiner has refused to Examiner claim 1 and other claims on their merits because the claim is broad and encompasses more than one patentably distinct invention. Although the Examiner has not made a "rejection" of any claims, the Examiner has deprived applicants of their right to an examination on the merits of the claims and thus has deprived applicants' of due process. This right to an examination was specifically addressed by the CCPA in In re Weber as follows:

> Logically, this is not a sufficient excuse for refusing to examine a claim on its merits for compliance with 35 USC 101, 102, 103, and 112. None of those statutory sections, of course, justifies a refusal to examine.
>
> The only justification or statutory authority put forward for refusing to examine is under 35 USC 121. ... So the discretionary power to limit one application to one invention is no excuse at all for refusing to examine a broad generic claim — no matter how broad, which

> means no matter how many independently patentable inventions may fall within it.
>
> Of course a broad claim may be unpatentable for any number of reasons, but we are not here dealing with a question of patentability under the statute but with a refusal to examine.

(Emphasis in the original) Rich, Judge, concurring 198 USPQ at 333-334.

The Examiner cites 35 U.S.C. § 101 for the proposition that an applicant can obtain "one patent per invention" (Final Action mailed September 15, 2003, page 3, bottom of page). 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The Examiner appears to take the position that Applicant is entitled to one patent as defined by the Examiner, whereas Applicants take the position that they are entitled to a patent as defined by the inventors. Applicants (not the Examiner) have the right to determine the scope of the claimed invention, *In re Wolfrum*, 486 F.2d 588, 179 USPQ 620, 622 (CCPA 1973) and In re Weber, 198 USPQ 328, 331 (CCPA 1978). For the foregoing reasons, it is submitted that applicants are being deprived of due process by refusal of the Examiner to examine the claims presented by applicant.

B. The Action of the Examiner is contrary to 35 U.S.C. § 112, second paragraph, which requires an applicant to define an invention as he/she contemplates it.

35 USC 112, second paragraph, states that "the specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as the invention". According to *In re Wolfrum*, 486 F.2d 588, 179 USPQ 620, 622 (CCPA 1973) and *In re Weber*, 198 USPQ 328, 331 (CCPA 1978), 35 USC 112, second paragraph, not only is a requirement imposed on an applicant, it also gives an inventor a right to claim an invention however he/she contemplates it. This basic right of an applicant, to

claim an invention as he/she sees fit, cannot be taken away by the Examiner under the guise of a requirement for restriction and/or election of species because such action expressly contradicts 35 USC 112, second paragraph.

C. The Action of the Examiner is contrary to *In re Weber*.

The case law permits restriction between groups of claims, not within a single claim. In this regard, *In re Weber*, 198 USPQ 331 (CCPA 1978), states

> An applicant is given, by the statute, the right to claim his invention with the limitations he regards as necessary to circumscribe that invention...
>
> As a general proposition, an applicant has a right to have *each* claim examined on the merits.... If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification.
>
> It is apparent that §121 provides the Commissioner with the authority to promulgate rules designed to *restrict* an *application* to one of several claimed inventions when those inventions are found to be "independent and distinct." It does not, however, provide basis for an examiner acting under the authority of the Commissioner to *reject* a particular *claim* on that same basis.
>
> ...We hold that a rejection under §121 violates the basic right of the applicant to claim his invention as he chooses.... (198 USPQ at 331-332)
>
> The fault in the PTO position is that it overlooks the obvious fact that almost any reasonably broad claim "embraces" or "covers" a multiplicity of inventions, in the sense of "dominating" them, which inventions might be separately patentable if and when presented in separate applications. Logically, this is not a sufficient excuse for refusing to examine a claim on its merits for compliance with 35 USC 101, 102, 103, and 112. None of those statutory sections, of course, justifies a refusal to examine.
>
> The only justification or statutory authority put forward for refusing to examine is under 35 USC 121. There is nothing therein, however, to excuse a refusal to examine an elected invention or an applicant's generic (broad) claim reading thereon, notwithstanding the generic claim reads on nonelected

> inventions and possibly many others, all potentially separately patentable.... So the discretionary power to limit one application to one invention is no excuse at all for refusing to examine a broad generic claim — no matter how broad, which means no matter how many independently patentable inventions may fall within it.
>
> Of course a broad claim may be unpatentable for any number of reasons, but we are not here dealing with a question of patentability under the statute but with a refusal to examine.

(Emphasis in the original) Rich, Judge, concurring 198 USPQ at 333-334.

The Examiner in this application is clearly refusing to examine the full scope of a broad claim. This is expressly prohibited by *In re Weber*.

D. The Action of the Examiner is contrary to 37 CFR 1.146 and MPEP § 803.02

37 C.F.R. 1.146 states that if an application contains a generic claim (such as claim 1 in the present application) and claims to more than one patentably distinct species, the Examiner may require the applicant to elect a species of his/her invention to which the claims will be restricted "if no claim to the genus is allowable". However, in the present case, the Examiner is requesting the applicant to restrict the claims prior to a finding that the generic claims are not allowable. This is not authorized by 37 C.F.R. 1.146. According to 37 C.F.R. 1.146, the Examiner must examine the generic claim in this application (Claim 1) and a reasonable number of species claims.

It is submitted that the Examiner has not followed MPEP § 803.02 which states in part:

> This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be

found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability....

...The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim.... (Emphasis added.)

MPEP § 803.02 requires the Examiner to search and examine the Markush-type claim until an unpatentable species is discovered, even if the claim contains independent and distinct inventions. The fact that the various compounds may be classified in different subclasses by the USPTO and that different fields of search may be involved does not mean that the Markush group is improper, In re Brouard, 201 USPQ (BNA) 538, 540 (Pat. & Trademark Off. Bd. App. 1977). Therefore, the entire scope of claim 1 should be examined. To the extent that the Code of Federal Regulations (particularly 37 CFR 1.142 and 1.146) and the MPEP are being interpreted in a manner inconsistent with the statutory law (35 USC and due process) and the cases cited in this petition, the regulations of the PTO and the procedures suggested in the MPEP are invalid and should be withdrawn by the USPTO.

V. CONCLUSION

For the foregoing reasons, the Commissioner is requested to grant the relief requested in Section II above.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 07-1392 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

Robert H. Brink

Robert H. Brink
Attorney for Applicants
Registration No.: 36,094

Date: October 28, 2003

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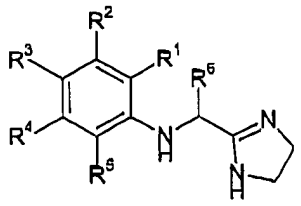
Appendix 1

1. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof,

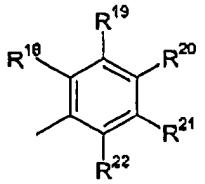


(I)

wherein R^2, R^3, R^4, and R^5 are independently H, halogen, -OH, -C_{1-3}alkyl, -C_{1-3}alkoxy, -SC_{1-2}alkyl, or -CF_3, with the proviso that at least 2 of R^2, R^3, R^4, and R^5 are H;

R^6 is H or -CH_3;

R^1 is -$S(O)_nR^7$ where n is 1 or 2, -$S(O)_2NHR^8$, -$C(O)R^9$, -$NR^{14}R^{15}$, -$C(R^{17})$=NOR^{16},

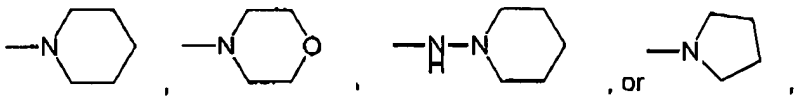


or a 5, 6, or 7 membered heteroalkyl or heteroaryl group optionally substituted with 1 or two groups selected from the group consisting of the following substituents for carbon: C_{1-3}alkyl, -CH_2CF_3, -CF_3, F, Cl, C_{1-2}alkoxy, C_{1-2}thioalkyl, and the following substituents for nitrogen: C_{1-3}alkyl and -CH_2C_{1-2}fluoroalkyl;

R^7 is C_{1-3}alkyl or C_{1-2}fluoroalkyl;

R^8 is C_{1-3}alkyl or -CH_2C_{1-2}fluoroalkyl;

R^9 is C_{1-3}alkyl optionally substituted with 1-3 fluorine atoms, -$NR^{10}R^{11}$, -$NHNR^{12}R^{13}$, -$CH_2SO_2CH_3$,



R^{10} is H or C_{1-2}alkyl;

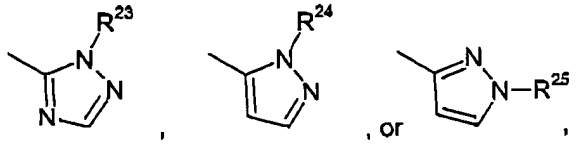
R^{11} is H, cyclopropyl, cyclopropylmethyl, C_{3-6}alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C_{1-6}alkyl optionally substituted with hydroxy, C_{1-3}alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R^{11} that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen;
R^{12} is H or C_{1-2}alkyl;
R^{13} is H, C_{3-5}cycloalkyl, cyclopropylmethyl, $-SO_2CH_3$, $-C(O)CH_3$, C_{3-6}alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C_{1-6}alkyl optionally substituted with hydroxy, C_{1-3}alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R^{13} that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen,;
R^{14} is H or C_{1-2}alkyl;
R^{15} is C_{3-5}cycloalkyl, cyclopropylmethyl, C_{3-6}alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C_{1-6}alkyl optionally substituted with hydroxy, C_{1-3}alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R^{15} that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen;
R^{16} is C_{1-2}alkyl;
R^{17} is H or C_{1-3}alkyl;
R^{20} is H; and
R^{18}, R^{19}, R^{21}, and R^{22} are independently H, halogen, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-SC_{1-2}$alkyl, or $-CF_3$ with the proviso that at least one of R^{18}, R^{19}, R^{21}, or R^{22} is other than H.

2. A compound of Claim 1 wherein R^2, R^3, and R^5 are H or F.

3. A compound of Claim 2 wherein R^4 = H, F, Cl, $-OCH_3$, or $-CH_3$.

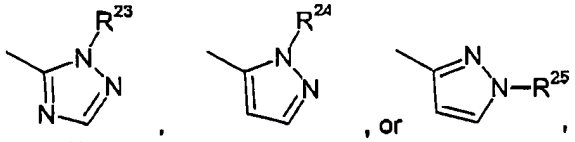
4. A compound of Claim 3 wherein R^6 is H.

5. A compound of Claim 4 wherein R^1 is $-S(O)_nR^7$, $S(O)_2NHR^8$,



where R^{23} is H, C_{1-3}alkyl, or 2,2,2-trifluoroethyl, R^{24} is H, C_{1-3}alkyl, or 2,2,2-trifluoroethyl, and R^{25} is H, methyl, or ethyl.

6. A compound of Claim 5 where R^1 is



where R^{23} is isopropyl or 2,2,2-trifluoroethyl, R^{24} is methyl or ethyl, and R^{25} is methyl, or ethyl.

7. A compound of Claim 5 wherein R^1 $S(O)_2NHR^8$.

8. A compound of Claim 7 wherein R^8 is CH_3.

9. A compound of Claim 5 wherein R^1 is $-S(O)_nR^7$.

10. A compound of Claim 9 wherein n is 2 and R^7 is CH_3.

11. A compound of Claim 1 selected from the group consisting of
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-propylbenzamide,
N-cyclopropyl-2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]benzamide,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzamide,
{2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]phenyl}(4-morpholinyl)methanone,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N,N-diethylbenzamide,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-ethyl-N-methylbenzamide,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methyl-N-propylbenzamide,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1,3-oxazol-5-yl)aniline,
1-{2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]phenyl}-1-ethanone,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(2-pyrazinyl)aniline,

N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(2-methyl-1,3-thiazol-4-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrazol-3-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrazol-5-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzenesulfonamide,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrrol-2-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-3-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-5-yl)aniline,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-ethylbenzenesulfonamide,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrrol-2-yl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-(2,2,2-trifluoroethyl)-1H-1,2,4-triazol-5-yl]aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(ethylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-fluoro-2-(methylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-chloro-2-(methylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-methyl-2-(methylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-methoxy-2-(methylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-isopropyl-1H-1,2,4-triazol-5-yl]aniline, and pharmaceutically acceptable salts and solvates thereof.

12. A compound of Claim 1 selected from the group consisting of
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-fluoro-2-(methylsulfonyl)aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-5-yl)aniline,
2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzenesulfonamide,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-(2,2,2-trifluoroethyl)-1H-1,2,4-triazol-5-yl]aniline,
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline, and
pharmaceutically acceptable salts and solvates thereof.

13. A compound of Claim 1 selected from the group consisting of
N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline and
pharmaceutically acceptable salts and solvates thereof.

14. A compound of Claim 1 wherein said compound is an alpha-1A agonist.

15. A method for prevention or treatment of an alpha-1A mediated disease or condition comprising administration of a therapeutically effective amount of a compound of claim 14.

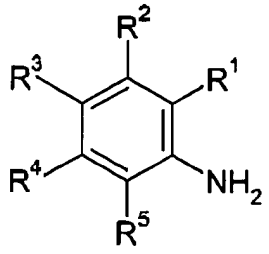
16. The method of Claim 15 wherein said disease or condition is urinary incontinence, nasal congestion, priapism, depression, anxiety, dementia, senility, Alzheimer's, deficiencies in attentiveness and cognition, and eating disorders such as obesity, bulimia, or anorexia.

17. The method of Claim 15 wherein said disease or condition is urinary incontinence.

19. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1.

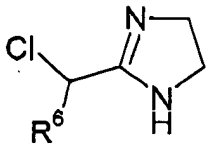
20. A pharmaceutical composition according to Claim 19 further comprising a pharmaceutically acceptable diluent or carrier.

24. A process for preparing a compound as claimed in claim 1 which comprises reacting a compound of formula II:



(II)

with a compound of formula III:



. HCl

(III)

25. A process as claimed in Claim 24 wherein the reaction is carried out at a pH in the range of from 3.0 to 4.0.

26. A process as claimed in Claim 25 wherein the reaction is run in a protic solvent.

27. A process as claimed in Claim 26 wherein said protic solvent is selected from the group consisting of methanol, ethanol, methoxyethanol, isopropanol, butanol, and phenol.

28. A process as claimed in Claim 27 wherein the protic solvent is 2-butanol.

29. A process as claimed in claim 28 wherein the reaction is run at a temperature or temperatures of from 80 to 140°C.